Complete nucleotide sequence of a highly infectious avian leukosis virus

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Submitted December 4, 1991 GenBank accession no. M37980

Rous sarcoma virus (RSV) is unique in that it is the only retrovirus competent for both replication and *in vitro* cell transformation. Most strains of RSV also contain two types of viruses which are defective for either transformation (*td*) or replication (*rd*). The RSV*td* present in stocks of RSV seem to be indistinguishable from avian leukosis viruses (ALV) (1). These ALV viruses can function as helpers for *rd* viruses by providing *gag*, *pol* and *env* functions in *trans* (2). Furthermore, original stocks of avian (ALV, RSV), murine (MLV) and human (HIV) retroviruses have been shown to contain a wide variety of virus variants with limited or extended capabilities of replication (1).

Here we report the complete nucleotide sequence of a highly infectious ALV of subgroup A (3) (Genbank accession number M37980). A recombinant plasmid DNA containing the infectious ALV provirus (plasmid pLADI) was constructed and transfected into avian cells. As shown in figure 1, ALV rapidly spreads in the cell culture and virus titer was as high as 10^5 iu/ml one day after transfection while that of RSV-PrC was less than 10^1 iu/ml (4).

The genomic RNA is 7286 nucleotides (nt) long and its genetic organization closely resembles that of replication competent retroviruses with the three long open reading frames *gag*, *pol* and *env* flanked by the 5′ and 3′ untranslated sequences. The LTR is 325 nt long with U3, R and U5 containing the inverted repeats for integration, the enhancers, the CAT and TATA boxes, and the poly(A) signal. The primer binding site specific for primer $tRNA^{Trp}$ and the polypurine track flank the LTR. The integration site is highly rich in A:T base pairs with a duplication (CATTTT) of chick cell DNA. The dinucleotides TG/CA are at the end of the integrated provirus.

Comparison with the sequences of RSV-PrC (5) and of known regions of RSV-SRA, RSV-SRD, RAV-50 and *evl* (6–8) indicates that this ALV probably results from multiple recombinations (9) since (I) R, U5 and U3 are identical to those of RSV-SRA, (II) the leader and 5′ *gag* with the encapsidation and RNA dimerisation sequences (10), and the 3′ *gag* corresponding to the nucleocapsid protein NCp12 domain seem to be unique to this ALV, (III) *gag* from positions 537 to 1066 is identical to *evl*, (IV) *pol* differs by only three conservative changes from that of RSV-PRC, (V) *env* is identical to that of RSV-SRA and (VI) the 3′ non coding sequences Z, F1 and PPT are identical to those of RAV 50. According to preliminary genetic and biochemical data, the major changes seen in the virion proteins MAp19, being of the β-form like its *evl* homolog, and NCp12, being more basic and with 8 prolines instead of 5 in RSV-PrC, are probably required for the high infectivity of this ALV isolate.

ACKNOWLEDGEMENTS

We thank C. Méric for providing the pAPrC plasmid. This work was supported by a grant from the ANRS, and a predoctoral fellowship to E.B. from the ARC.

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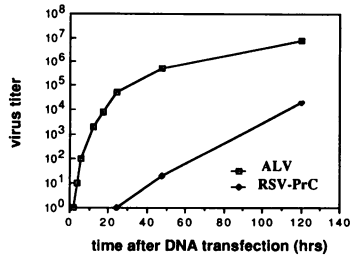

Figure 1. Virus titer of ALV produced early after DNA transfection. Plasmids pLADI and pAPRC (4) were transfected in chick embryo fibroblasts using DEAE dextran (4). Virus infectivity, in infectious units per ml of medium, was monitored by the end point dilution methodology and reverse transcriptase assay (3, 4). Open squares, pLADI (ALV). Closed squares, pAPrC (RSV).

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